UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,870	08/06/2001	Bernhard Palsson	PALSSN.002C1	1729

7590 02/22/2006

McDERMOTT WILL & EMERY LLP
4370 La Jolla Village Drive
Suite 700
San Diego, CA 92122

EXAMINER	
ALLEN, MARIANNE P	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,870	PALSSON, BERNHARD	
	Examiner	Art Unit	
	Marianne P. Allen	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-54,56-62,64 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-54, 56-62, 64-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/29/05 has been entered. Claims 1-48, 55, and 63 have been cancelled. Claims 49-54, 56-62, and 64-64 are under consideration.

Applicant's arguments filed 11/29/05 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 49-54, 56-62, and 64-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and enablement requirements. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and/or as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is both a new matter and enablement rejection.

Claim 49 now recites "obtaining a DNA sequence of a genome." As set forth in the prior Office action, this amendment is considered to be new matter. Applicant argues that the specification contemplates less than the entire genome by pointing to parts of the specification that disclose "most of all of the metabolic reactions," "most or all of the genes," and "nearly the entire." However, the claims as amended do not reflect these concepts and thus still embrace new matter. The claims in the most limited embodiment require a single DNA sequence of a genome. The claims embrace less than most or nearly all of the genes. Applicant is advised that inclusion of language such as "most" or "nearly" in the claims would be indefinite as it doesn't make clear what percentage or number of sequences must be obtained or have function assigned to meet the limitations of the claims.

Claim 53 remains new matter for reasons of record. Claim 53 is directed to a method of producing an *in silico* representation of a microbe in a computer. Applicant points to page 9, lines 11-17, with respect to Figure 2, steps 50-58 stating that the genome specific stoichiometric matrix is the fundamental representation of a genomically and biochemically defined genotype. Applicant's arguments are not persuasive. This remains inconsistent with Figure 2 which clearly states that production of the *in silico* representation requires additional steps 60, 62, and 64. Claim 53 as presently written does not end at production of the genome specific stoichiometric matrix but includes additional steps to produce the *in silico* representation. Claim 53 does not require formulating the general linear programming problem representing the *in silico* strain of

the organism (step 64). The concept set forth in step 64 is not synonymous with combining the metabolic demands and uptake rates with the stoichiometric matrix as recited in claim 53. Applicant's originally filed specification does not reasonably convey to one of ordinary skill in the art that the invention as presently claimed was contemplated. The originally filed specification does not refer to the stoichiometric matrix alone as the *in silico* representation of a microbe. See also page 10, lines 8-11, and page 12, line 27, through page 13, line 1, of the specification for disclosure as to what constitutes the *in silico* representation of a microbe.

Basis for the methods of claims 57-61 is still not seen, particularly repeating steps a) to d) and providing only metabolic genes (as opposed to selecting the subset that are metabolic genes from the ORF's found in the whole genome). Applicant's arguments are not persuasive. Applicant has not pointed to basis is the specification where the recited steps of the method are disclosed or contemplated. Page 7, lines 27-29; page 8, lines 4-5; and pages 9-10 do not disclose the steps (including all limiations and order) of claims 57-61.

The rejection with respect to claim 49 is maintained for reasons of record. Again, **to the degree that claim 49 is intended to assign function to every open reading frame identified in the microbial genome,** the specification is not enabling for the reasons set forth in the prior Office action. Note that even according to applicant's arguments "most" or "nearly" all open reading frames should have function assigned. See above.

Contrary to applicant's assertion on page 12 of the response, the prior Office action did not deny any weight to the proffered evidence of the Subramanian declaration. The

Subramanian declaration admits in paragraph 4 that all open reading frames in a genome cannot be automatically assigned function. There is no provision in the claims for assigning only those with a certain (unspecified) level of homology to known proteins. The claims require assignment of function to all or most or nearly all, not some, open reading frames.

Paragraph 8 of the declaration discusses assigning gene function for *E. coli*, in particular. However, the claims are directed to any microbe not just *E. coli*.

With respect to paragraph 10, there is no evidence presented in support of the assertion that "any experimentation necessary to obtain a sequence homology search and assign a function based on homology to a known gene was predictable and routine." The remainder of the paragraph outlines that criteria are selected by the user and an assertion of common practices with regard to E-values. These criteria and E-values are not limitations of the claims. Nor does this establish that the art at the time of the invention had known or accepted criteria by which function was assigned.

Again, claims 49 and 57 require being able to discriminate between a metabolic gene and a non-metabolic gene. One must be able to determine those ORFs "involved in cellular metabolism" by their assigned function. However, this does not clearly demarcate those genes or ORFs intended to be included or excluded. Page 8 provides a non-limiting list as to what was intended and the degree of "involvement" is not made clear. As such, one of ordinary skill in the art would not have known exactly which sequences to include or exclude, with the exception of claims 51 and 59. From the perspective that any gene can affect the overall function of the cell, most, if not all, genes could be considered to be involved in cellular metabolism. Applicant's arguments do not address the fact that the specification disclosure of the metes and

bounds of "metabolic gene" is non-limiting and applicant does not provide a limiting definition well-known to one of ordinary skill in the art at the time of the invention for a "metabolic gene."

Again as set forth in the prior Office action, the specification does not provide guidance on how assignment of function would then provide the metabolic reaction of the candidate metabolic gene. That is, assigning the function of a kinase based upon homology does not provide the substrate and product of the reaction. The specification provides absolutely no guidance as to how these should be determined. While page 8, discusses reviewing biochemical literature and available experimental data, this is considered to require undue experimentation given the breadth of the claims which are directed to any microbe and appear to embrace all genes of the microbial genome. Applicant attached the Table of Contents from Stryer et al.; however, the claims are not limited to glycolysis or particular known pathways. The claims are not limited to known substrates and products.

Claim 54-55 and 64-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 54 and 65 are confusing for reasons of record and as discussed above with respect to the requirement of producing an *in silico* representation in the new matter rejection.

Claim Rejections - 35 USC § 102

Claims 49-51, 53-59, and 61-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Schilling et al. (Biotech. Prog., 15(3):288-295, May/June 1999, of record).

This rejection is maintained for reasons of record. As the claims as presently written embrace new matter, applicant is entitled to only the instant filing date of 8/6/01 and not the filing date of parent application 09/243,022.

Claim Rejections - 35 USC § 103

Claims 52 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schilling et al. al. (Biotech. Prog., 15(3):288-295, May/June 1999, of record).

This rejection is maintained for reasons of record. Schilling remains valid prior art.

Claims 49-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Blattner et al. (Science, 1997, of record), Pennisi (Science, 1997), Edwards et al. (Abstracts of Papers, American Chemical Society, 213(1-3):BIOT 50, San Francisco, April 13-17, 1997), and Pramanik et al. (Biotechnology and Bioengineering, 1997, of record).

This rejection is maintained for reasons of record.

Applicant argues that Pramanik et al. teaches away from using models that are not produced from existing biochemical information. This is not agreed with. Page 4 of the specification discusses Pramanik et al. However, these concerns are not applicable with respect to the art applied as biochemical information was known at the time of the invention for the organisms suggested.

Again, Edwards et al. discloses flux balance analysis of a metabolic network for *H. influenzae* based on homology of putative proteins with those encoded by the known part of the *E. coli* genome. Thus, the information is rooted in known biochemical information. Blattner,

Pennisi, and Pramanik et al. establish that *E. coli* and *H. influenzae* biochemical information would have been well known at the time of the invention.

It is maintained that it would have been obvious to produce a stoichiometric matrix and *in silico* model of the microbes *E. coli* and *H. influenzae* according to Pramanik et al. using the known genome sequence, ORFs, and metabolic genes for these microbes as disclosed by Blattner et al. and Pennisi et al. (where function has been assigned by using homology and tools such as BLAST). Such models clearly would have been of interest and within the skill of the art to produce as seen by Edwards et al. One would have been motivated to produce the stoichiometric matrix and *in silico* model in order to better understand microbial metabolism and provide more robust models of metabolism. The art applied is analogous and looks to further characterize the same microbial metabolic systems. It is maintained that it would have been obvious to combine the teachings of the prior art in order to arrive at the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne P. Allen
Primary Examiner
Art Unit 1647

2/21/06

mpa